

High Dispersion of Ventricular Repolarization After an Implantable Defibrillator Shock Predicts Induction of Ventricular Fibrillation As Well As Unsuccessful Defibrillation

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- OBJECTIVES** To test the hypothesis that post-shock dispersion of repolarization (PSDR) is higher in T wave shocks that induce ventricular fibrillation (VF) than in those that do not, as well as in implantable cardioverter defibrillator (ICD) defibrillation shocks which fail to terminate VF when compared with those that are successful.
- BACKGROUND** Ventricular fibrillation has been linked to the presence of dispersion of repolarization, which facilitates reentry. Most of the studies have been done in animals, and the mechanism underlying the generation and termination of VF in humans is speculative and remains to be determined.
- METHODS** Monophasic action potentials (MAPs) were recorded simultaneously from the right ventricular outflow tract (RVOT) and the right ventricular apex (RVA) in 27 patients who underwent implantation and testing of an ICD. T wave shocks were used to induce VF while the termination was attempted using internal defibrillator shocks. The post-shock repolarization time (PSRT) was measured in both the RVA and RVOT MAPs, and the difference between the two recordings was defined as the PSDR. The averages of PSDR were compared between the successful and unsuccessful inductions and terminations of VF.
- RESULTS** T wave shocks that induced VF generated a greater PSDR (93.4 ± 85.1 ms) than the unsuccessful ones (45.1 ± 55.9 ms, $p < 0.001$). On the other hand, shocks that failed to terminate VF were associated with a greater PSDR (59.9 ± 41.2 ms) than shocks that terminated VF (21.1 ± 20.1 ms), $p < 0.001$.
- CONCLUSIONS** A high PSDR following a T wave shock is associated with induction of VF; while following a defibrillating shock, it is associated with its failure and the continuation of VF. Conversely, a low PSDR is associated with failure of a T wave shock to induce VF and successful termination of VF by a defibrillating shock. (J Am Coll Cardiol 2000;35:422-7) © 2000 by the American College of Cardiology

Electrical shocks applied during ventricular repolarization are able to induce ventricular fibrillation (VF) (1,2). In recent years, T wave shocks have been widely used to induce VF in patients with an implantable cardioverter defibrillator (ICD) (3,4). A presumed mechanism of induction of VF by a T wave shock is the initiation of reentrant waveforms from

functional conduction block within the ventricular myocardium (5-8).

However, electrical shocks are the mainstay for the treatment of VF. Multiple mechanisms have been offered to explain electrical defibrillation, such as depolarization of a critical mass of myocardium (9) or prolongation of the action potential duration which might stop the progression of the reentrant electrical wavelets by increasing the refractory period (10).

The electrophysiological effect of a shock, and its impact on the action potential and the dispersion of repolarization have been shown in different studies (11-14). However, the association of the dispersion of repolarization with both the

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Abbreviations and Acronyms

ICD	= implantable cardioverter defibrillator
J	= joules
MAP	= monophasic action potential
PSDR	= post-shock dispersion of repolarization
PSRT	= post-shock repolarization time
RVA	= right ventricular apex
RVOT	= right ventricular outflow tract
VF	= ventricular fibrillation

induction of VF by a T wave shock and failure to terminate it by an electrical shock remains to be proven.

Implantable cardioverter defibrillator testing offers the opportunity to study the induction and termination of VF in patients under controlled conditions. Monophasic action potentials (MAPs) from the right ventricular apex (RVA) and the right ventricular outflow tract (RVOT) were recorded during the above inductions and terminations of VF. The degree of dispersion of repolarization between these two areas following the electrical shock were measured and correlated with successful and unsuccessful inductions and terminations. We sought to determine if there is a significant association between a high dispersion of repolarization and the success of initiation of VF, on one hand, and the failure to terminate it, on the other hand.

METHODS

Patient population. The study included 27 patients who were referred to the Veterans Administration Medical Center, Washington, DC, for an ICD implant, following an episode of sudden cardiac death or hemodynamically significant ventricular tachycardia. Twenty-six were men, 25 had a documented myocardial infarction in the past and 25 had depressed ejection fraction (<40%). Medications taken by the patients, including antiarrhythmic agents, were continued before and during the study. Informed consent was obtained from each patient in compliance with the Human Research Committee requirements.

Preparation. Patients underwent ICD implantation using the nonthoracotomy approach in the clinical electrophysiology laboratory. Under local anesthesia, combined with a light general anesthesia (propofol), two defibrillator leads were introduced via the left subclavian vein and positioned in the RVA and the superior venae cava, respectively. These two leads were connected to an ICD generator (Medtronic or CPI) placed in a subcutaneous pocket, which was created in the thoracic or abdominal area. Before testing the device, two MAP catheters with pacing capabilities (7F quadripolar Franz combination catheter, EP Technologies) were introduced via the femoral vein and placed in contact with the endocardial surface of the RVOT and the RVA, respectively. The MAP recordings have been shown to reproduce reliably the local cellular action potential time course (15). A

twelve lead ECG, as well as the MAP tracings, were recorded continuously during the study on a Bard system (Boston, Massachusetts) and stored on a hard drive and optical disks. Vital signs were continuously monitored and an anesthesiologist was present during the whole procedure.

Study protocol. The study was conducted according to a standard protocol for determining defibrillation threshold at implant. The ICD lead placed in the RVA was used to pace the ventricle at twice the pacing threshold, at a cycle length of 400 or 600 ms. After 8 or 10 pacing cycles, an electrical shock of 0.6 to 2 J was applied on the ascending part of the T wave. If it failed to induce VF, the shock was repeated after changing the coupling interval by 10 ms and the shock energy. If this failed, the attempts were repeated with variable combination of coupling intervals and shock energies (0.6 to 2 J). When VF was induced, the episode was terminated by an internal electrical shock delivered by the ICD, at a predetermined energy of 35 J. If this failed, an external rescue shock of 360 J was delivered to terminate VF. A period of 5 min was allowed to elapse. Another induction of VF was attempted using the same T wave shock. When VF was induced, the episode was terminated with an internal shock of 30 J. A rescue shock was applied if necessary. Five minutes were allowed to elapse and the sequence was repeated with a 5 J decrement in the internal defibrillator shock energy. The study was stopped at 5 J defibrillation.

Data analysis. All measurements were done manually on a Bard display screen, using electronic calipers. For each episode of T wave shock induction and each internal defibrillation attempt, the following parameters were defined (Fig. 1): 1) the coupling interval, as the time between the upstroke of the MAP and the shock artifact, 2) the post-shock repolarization time (PSRT) as the time between the shock artifact and the maximum repolarization of the response generated by the shock, 3) the post-shock dispersion of repolarization (PSDR) as the difference between the PSRTs in the two MAP recordings.

Statistical analysis. Results were expressed as the mean \pm standard deviation. The mean PSDR of the T wave shocks that induced VF and the ones that failed were compared using an unpaired Student *t* test. The same test was used to compare the mean PSDR of the unsuccessfully and successfully defibrillating shocks. A *p* value of <0.05 was considered significant. All statistical evaluations were performed using a JMP software package (version 3.0.2, SAS Institute Inc.), run on an Apple Macintosh computer.

RESULTS

VF induction. In 27 patients, 308 T wave shocks ranging from 0.6 to 2 J were applied. Of these, 244 T wave shocks induced VF while 64 failed to do so. The T wave shocks that induced VF had a mean strength of 1.38 ± 1.01 J at a mean coupling interval of 281.87 ± 33.48 ms. The T wave

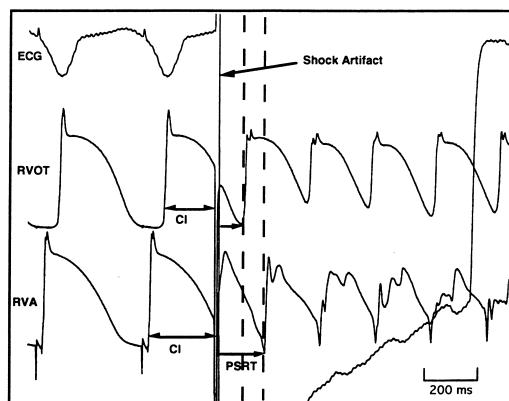


Figure 1. Measurements of the dispersion of repolarization (DR) between the right ventricular outflow tract (RVOT) and the right ventricular apex (RVA) following an electrical shock. Simultaneous recordings of the surface electrocardiogram (ECG), the monophasic action potential (MAP) in the RVOT and the MAP in the RVA. The coupling interval (CI) is the time between the upstroke of the MAP and the shock artifact. The post-shock repolarization time (PSRT) is the time between the shock artifact and the full repolarization following the shock. Post-shock DR (PSDR) is the difference between the PSRTs in the RVOT and RVA (time between the two dashed lines). This is an example of a successful induction of ventricular fibrillation (VF) by a T wave shock. Post-shock repolarization time in the RVA is 180 ms; PSRT in the RVOT is 90 ms. PSDR is 90 ms and is followed by VF.

shocks that failed to induce VF had a mean strength of 1.42 ± 0.65 J ($p = 0.739$) at a mean coupling interval of 282 ± 40.706 ms ($p = 0.8$).

Figure 1 depicts an example of a successful induction of VF. In this instance, the T wave shock encountered two different levels of repolarization in the RVOT and RVA,

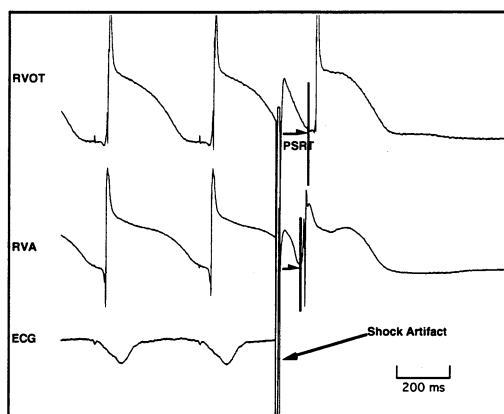


Figure 2. Simultaneous recordings of the electrocardiogram (ECG) and the monophasic action potential (MAPs) in the right ventricular outflow tract (RVOT) and right ventricular apex (RVA) during failed induction of ventricular fibrillation (VF). Post-shock repolarization time (PSRT) is 110 ms in the RVOT; PSRT is 95 ms in the RVA. The post-shock dispersion repolarization (PSDR) is 15 ms. The T wave shock generated one ventricular beat with no VF induction.

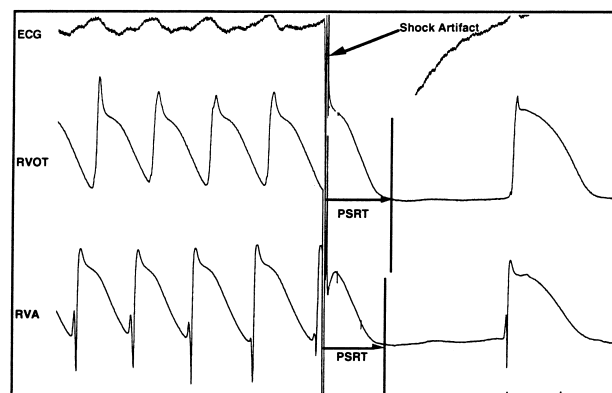


Figure 3. Simultaneous recordings of the ECG and the MAPs in the RVOT and RVA during successful internal defibrillation shock delivered by the implantable cardioverter defibrillator (ICD). The PSRT in the RVOT is 205 ms; the PSRT in the RVA is 200 ms. The PSDR is 5 ms with termination of VF. Abbreviations as in Figure 1.

respectively, producing a short PSRT in the RVOT and a much longer PSRT in the RVA. Subsequently, the PSDR was high with subsequent induction of VF.

Figure 2 shows an example of a failed attempt to induce VF. When the T wave shock was applied, the level of repolarization was similar in the RVOT and RVA. The result was the generation of a similar PSRT in the two recordings. The PSDR in this instance was low with no induction of VF.

The mean PSDR generated by the successful shocks (93.4 ± 85.1 ms) was significantly longer than the mean PSDR generated by the unsuccessful ones (45.1 ± 55.9 ms), with a $p < 0.001$ (Fig. 5).

Defibrillation. Two hundred of 244 episodes of induced VF required defibrillation with internal shocks ranging from 5 to 35 J. The mean shock strength did not differ signifi-

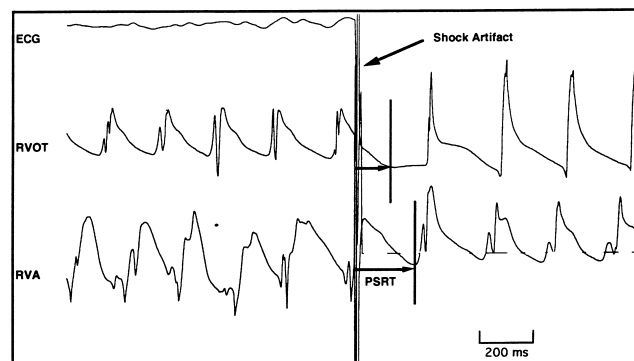


Figure 4. Simultaneous recordings of the ECG and the MAPs in the RVOT and RVA during failed internal defibrillation shock delivered by the implantable cardioverter defibrillator (ICD). The PSRT in the RVOT is 125 ms; the PSRT in the RVA is 210 ms. The PSDR is 85 ms. The VF persisted following the shock. Abbreviations as in Figure 1.

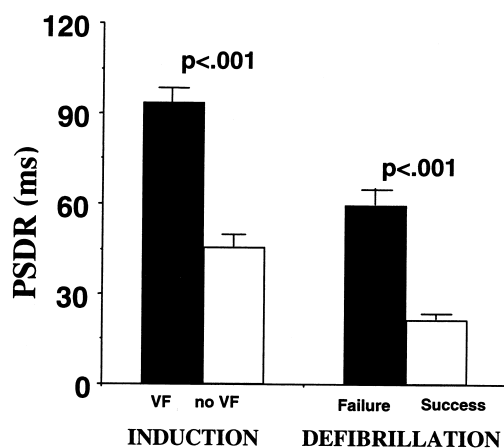


Figure 5. Post-shock repolarization time (PSDR) expressed as mean \pm standard error. **Left:** the PSDR generated by T wave shocks which induced ventricular fibrillation (VF) is significantly higher than the PSDR generated by T wave shocks which failed to induce VF. **Right:** the PSDR generated by the internal defibrillation shocks that failed to terminate VF is significantly higher than the PSDR generated by the successful defibrillation shocks.

cantly between the successful and unsuccessful defibrillations. Figure 3 depicts an example of successful defibrillation. The delivered shock produced similar PSRTs in the RVOT and RVA with the subsequent generation of a very short PSDR and the termination of the VF. In Figure 4, the electrical shock resulted in a longer PSRT in the RVA than in the RVOT. The PSDR generated in this instance was high with failure to terminate VF.

The mean PSDR generated by an internal defibrillation shock which failed to terminate VF (59.9 ± 41.2 ms) was significantly longer than the mean PSDR following successful defibrillations and termination of VF (21.1 ± 20.1 ms, $p < 0.001$) (Fig. 5).

DISCUSSION

This study analyzed the effect of T wave shocks and internal defibrillation shocks on the dispersion of repolarization between the RVOT and RVA. The main findings were that a high dispersion of repolarization is associated first with the induction of VF by a T wave shock and second with the failure of internal defibrillation. Conversely, a lower dispersion is associated with the failure of T wave shock to induce VF and with successful defibrillation.

Electrophysiological effect of an electrical shock. Many experimental studies in isolated cell preparations and animals have analyzed the effect of an electrical field on the action potential of the myocardium. Kao and Hoffman (16) showed in isolated myocardial tissue that stimuli applied during the refractory period extend the time course of repolarization, thereby creating prolongation of refractoriness. Tovar et al. (10) showed that the success of an electrical shock in terminating VF in the rabbit heart was

related to the degree of prolongation of the action potential by the shock. This prolongation and its extent depend on the coupling of the shock and its strength. The prolongation of the action potential, which extends the refractory period, would stop propagation of the multiple electrical wavelets of VF and was offered as a possible explanation for the mechanism of defibrillation. However, it did not explain the induction of VF by a shock in the vulnerable period or the absence of a correlation between the effect of an electrical shock on the action potential duration and its success in terminating VF. Later studies have shown that an electrical shock will induce different degrees of prolongation of the action potential, depending on the shock strength and the latency (11). This differential prolongation of repolarization will create areas of blockade to the electrical activation, a prerequisite for reentry. Although these studies showed that an electrical shock can create areas of electrical anisotropy, which could explain the induction of VF and the failure to terminate, it did not show a direct association between the dispersion of repolarization and the VF itself.

Experimental studies of dispersion. In our laboratory, we showed that a high dispersion of repolarization following an electrical shock determines its success in inducing VF. The post-shock dispersion was influenced by the shock timing and intensity (17). In the same study, we have shown that an electrical shock that approaches the upper limit of vulnerability produces a low dispersion, which could explain the failure to induce VF. Dillon (13) demonstrated that an electrical shock produced an action potential in partially depolarized myocardium. He hypothesized that the generation of a full action potential during VF will result in the homogenization of depolarization and subsequently the termination of the VF wavefront. Other studies have shown that an electrical shock will prolong depolarization and refractoriness. It explained the induction of VF by the creation of a temporary refractoriness, which would favor reentry, but it could not explain the discordance between the degree of prolongation of the action potential and the success of defibrillation (18). Human studies have suggested an association between dispersion of repolarization and torsade de pointes, spontaneous or iatrogenic, and the induction of ventricular tachycardia using one or multiple extrastimuli (19–21). Similarly, mapping studies showed the presence of electrical anisotropy during VF (22). However, there have been no studies in human correlating the induction or termination of VF by an electrical shock and the dispersion of repolarization generated by the shock.

Measuring dispersion of repolarization in the clinical laboratory. The simultaneous use of MAP catheters in the human heart during implantation and testing of ICDs offers an opportunity to study the initiation and termination of VF. We measured the PSRT in the RVA and RVOT and the PSDR after T wave and internal defibrillation shocks. Prolongation of refractoriness following a shock was measured using MAP catheters. In normal myocardium, the

relationship between refractoriness and action potential duration as measured by MAP is very close (23). However, we cannot rule out that ischemia during VF might have influenced this relationship.

Most of the experimental animal studies showed that the PSRT depends on the timing and strength of the shock. An electrical shock will produce prolongation of depolarization, which will increase gradually, when the shock is applied later in the repolarization (10,11). This could explain the fact that a similar degree of repolarization in the RVA and RVOT will produce similar PSRT following a T wave shock and subsequently a low PSDR. Our study showed that a high PSDR following a T wave shock is associated with the successful induction of VF while a lower PSDR is associated with the failure to induce VF. These results show that T wave shocks in humans may or may not produce a prolongation of the action potential, but the induction of VF is associated mostly with the generation of a high PSDR following the T wave shock. The dispersion of repolarization, which reflects a difference in refractoriness, creates a functional conduction block (24,25), which is a prerequisite for induction of reentry and VF (5-7).

Similarly, our study showed that defibrillating shocks would induce a variable PSRT in the RVOT and RVA depending on the degree of repolarization in these two sites at the time of the shock. Different PSRTs generate a high PSDR and are associated with the perpetuation of VF. Similar PSRTs generate a lower PSDR and are associated with the termination of VF.

Although a cause of effect was not established, the strong association of PSDR and VF shown by our study, combined with the understanding of the electrical reentry that underlies VF, strongly suggests that dispersion of repolarization is a prerequisite for the initiation and perpetuation of VF.

Study limitations. Our study was done in a predominantly male population with coronary artery disease and low ejection fraction. This may preclude the generalization of the results to nonischemic VF. For obvious ethical reasons, we limited the number of shocks delivered to the heart. This precluded the systematic measurement of a correlation between shock strengths, coupling intervals and amount of dispersion induced. For the same ethical reasons, the use of only two MAP catheters in the RVOT and RVA limited the measurements to these two areas and may have prevented the detection of further dispersion in the left ventricle or other areas of the right ventricle. However, the random distribution of dispersion of repolarization in VF makes it likely to detect it by any two random points chosen, such as the RVOT and RVA. This may explain the consistency of our findings among different patients.

Conclusions. T wave shocks generate variable degrees of prolongation of the action potential depending on the degree of repolarization of the myocardium. The creation of a high dispersion of repolarization will facilitate electrical re-entry by creating functional blocks and subsequently

favor the induction of VF. Ventricular fibrillation will be terminated by an electrical shock if the latter generates a low dispersion of repolarization, which would prevent the continuation of the re-entrant wavelets.

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